complementarity determining region (CDR) of an immunoglobulin light chain gene which comprises amplifying a CDR portion of the immunoglobulin gene by polymerase chain reaction (PCR) using a PCR primer oligonucleotide, said oligonucleotide having 3' and 5' termini and comprising:

a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;

b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene;

c) a nucleotide sequence between said 3' and 5' termini according to the formula:

$$[NNK]_n,$$

wherein N is independently any nucleotide, K is G or T, and n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto;

C1 cont'd

d) isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;

e) expressing the isolated library of mutagenized light chain genes in combination with one or more heavy chain genes to form a combinatorial antibody library of expressed heavy and light chain genes; and

f) selecting species of said combinatorial antibody library for the ability to bind a preselected antigen.

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24. (Amended) The method of claim 14 wherein said one or more immunoglobulin heavy chain genes is a library of heavy chain genes.

C2

25. (Amended) A method for producing an antibody combining

site in a polypeptide comprising inducing mutagenesis in a complementarity determining region (CDR) of an immunoglobulin light chain gene which comprises amplifying a CDR portion of the immunoglobulin gene by polymerase chain reaction (PCR) using a PCR primer oligonucleotide, said oligonucleotide having 3' and 5' termini and comprising:

a) a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene;

b) a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin gene; and

c) a nucleotide sequence between said 3' and 5' termini according to the formula:

$$[MNN]_n,$$

wherein N is independently any nucleotide, M is A or C, n is 3 to about 24, said 3' and 5' terminal nucleotide sequences having a length of about 6 to 50 nucleotides, or an oligonucleotide having a sequence complementary thereto;

d) isolating the amplified CDR to form a library of mutagenized immunoglobulin light chain genes;

e) expressing the isolated library of mutagenized light chain genes in combination with one or more heavy chain genes to form a combinatorial antibody library of expressed heavy and light chain genes; and

f) selecting species of said combinatorial antibody library for the ability to bind a preselected antigen.

34. (Amended) The method of claim 25 wherein said one or more immunoglobulin heavy chain genes is a library of heavy chain genes.